onco Bretagne

Journée scientifique

HÉPATO-BILIO-PANCRÉATIQUE

Dr Baptiste GIGUET - Hépatologie (SMF)

VENDREDI 22 MAI 2026
9H30 -16H00

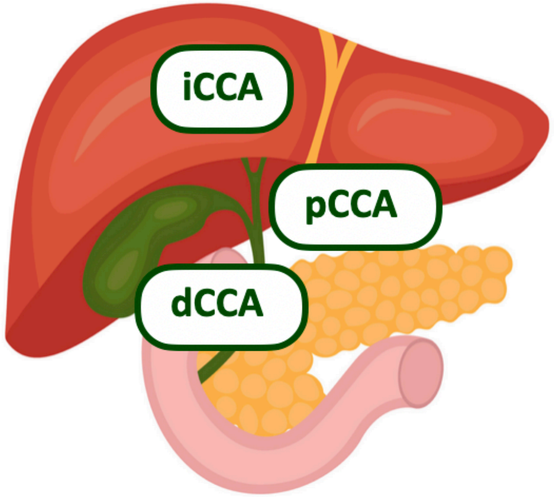
RENNES
CENTRE DES CONGRÈS
COUVENT DES JACOBINS
Place St Anne
35000 RENNES

Liens d’intérêt

- Chiesi (board)
- Gilead (orateur)
- Astellas (orateur)

Cholangiocarcinome et transplantation hépatique

- 2ème cause de tumeur hépatique primitive.
- Faible survie à 5 ans, même après résection.
- TH pour iCCA : survie médiocre 30% à 3 ans.
- Le cholangiocarcinome intra hépatique (iCCA) n'est pas une indication « classique » de transplantation hépatique (TH)



Goldstein RM et al. Am J Surg 1993
Pichlmayer R et al. World J Surg 1995
Becker NS et al. J Gastrointest Surg 2008
Mazzafero et al. J Hepatol 2020

Mme G, 44 ans

- Aucun ATCD notable
- Septembre 2023 : bilan de colique hépatique

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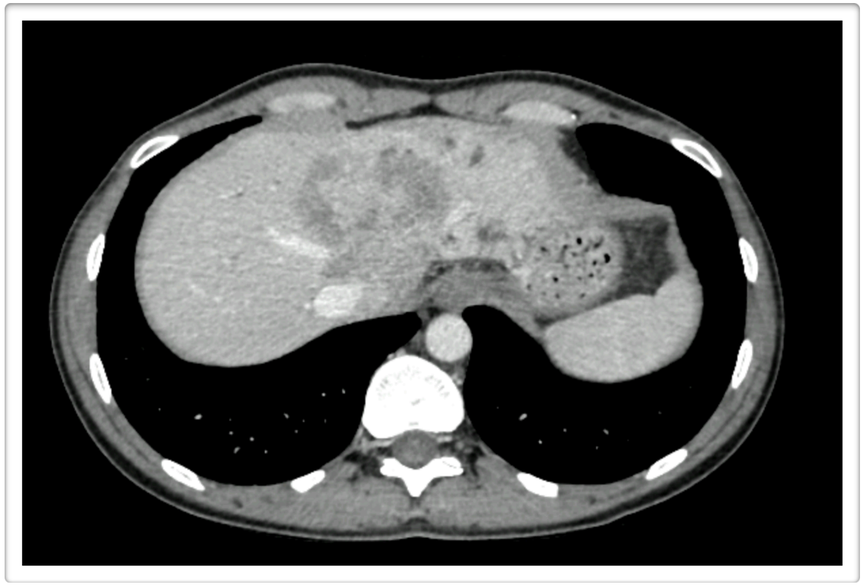
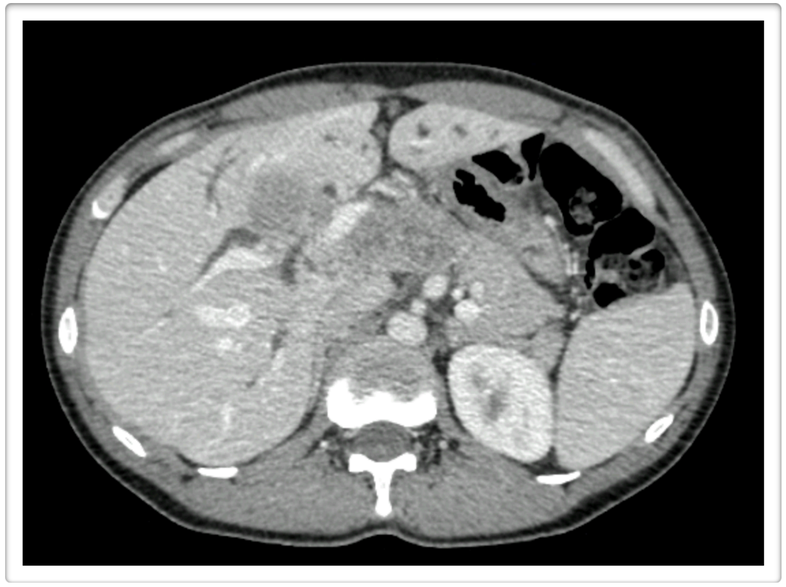
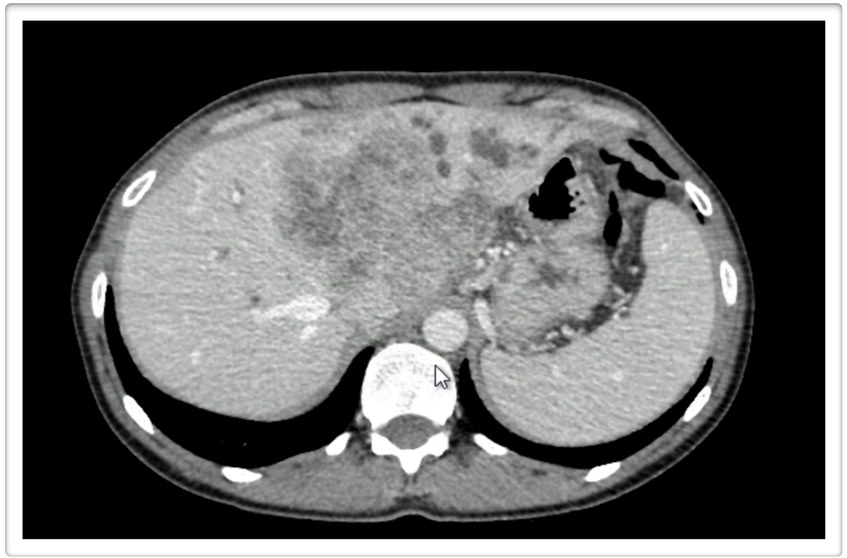






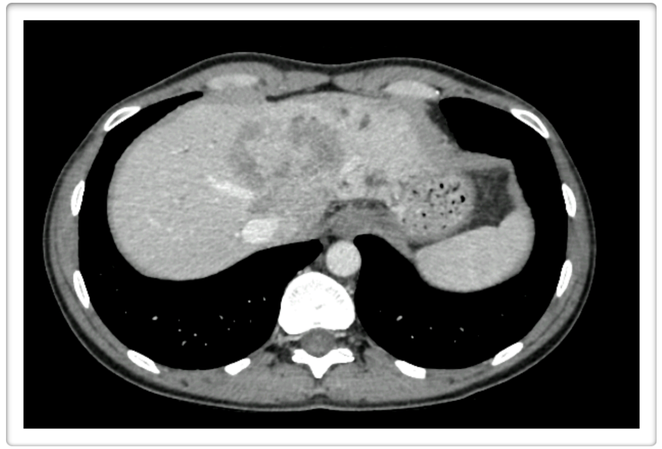
Mme G, 44 ans

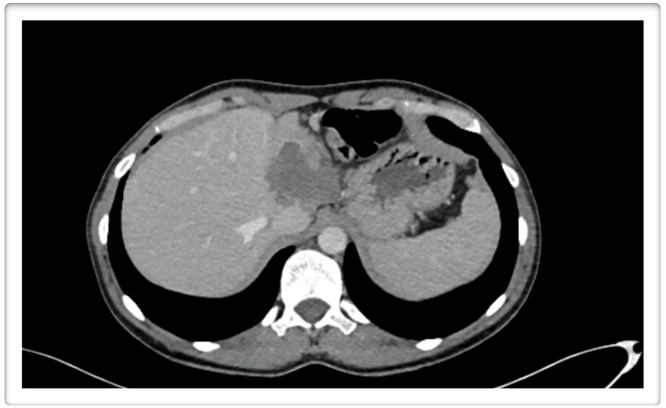
- Aucun ATCD notable
- Septembre 2023 : bilan de colique hépatique

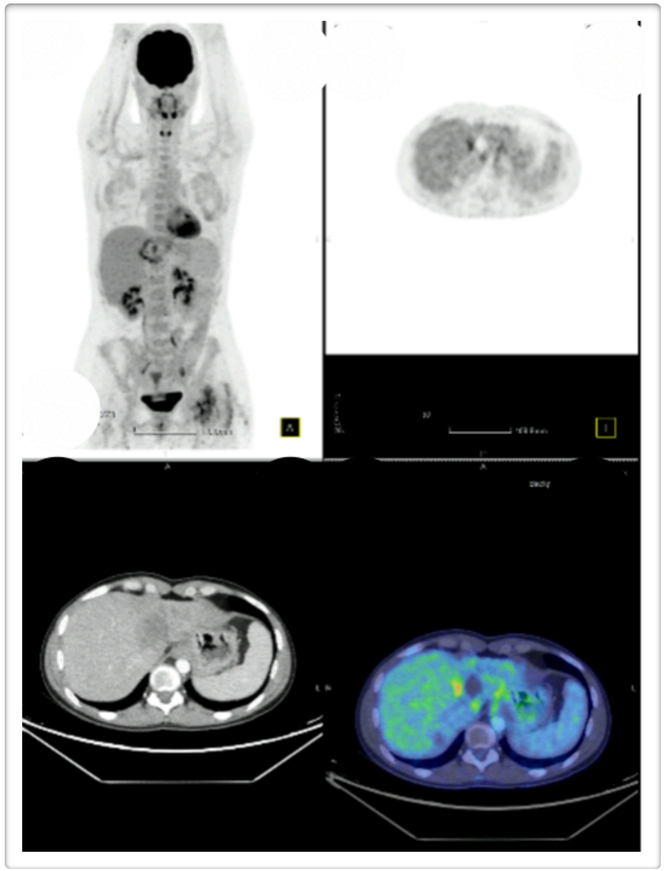
- Biopsie : ADK moyennement différencié orientant vers iCCA
- Variant NRAS muté
- Phénotype MSS,
- Absence de variants BRAF, HER II, IDH 1 ou 2, FGFR2 et 3

Mme G, 44 ans

09/23	diagnostic iCCA
10/23	Gemcis + Durvalumab
12/23	SIRT (Thérasphère Yttrium-90) Double injection (a.SIII et a.SIV et SII)
01/24	Excellente réponse partielle
04/24	RP, relai Durvalumab seul
07/24	RP mais non résécable, début BPTH
08/24	TEP TDM : absence d'extension extra hépatique
08/24	Picking GG négatif (2 prélevés)







Mme G, 44 ans

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10/24	Arrêt Durvalumab ; Reprise GEMCIS
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CONCLUSION :

1/ HEPATECTOMIE TOTALE :

La lésion observée macroscopiquement de 5.5 cm correspond à 99 % à des remaniements nécrotico-fibro-collagènes hyalinisés très peu inflammatoires.

On observe uniquement au niveau du collet de la vésicule biliaire, un foyer tumoral de 0.9 cm de plus grand axe, dont l'aspect histologique et le profil immunohistochimique vont dans le sens d'un cholangiocarcinome moyennement différencié.

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- IS initiale : CTC + CNI + MMF
- Réactivation CMV, arrêt MMF
- Intolérance évérolimus

- Monothérapie de tacrolimus
- 1 an post TH : absence de récidive

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Cholangiocarcinome et transplantation hépatique

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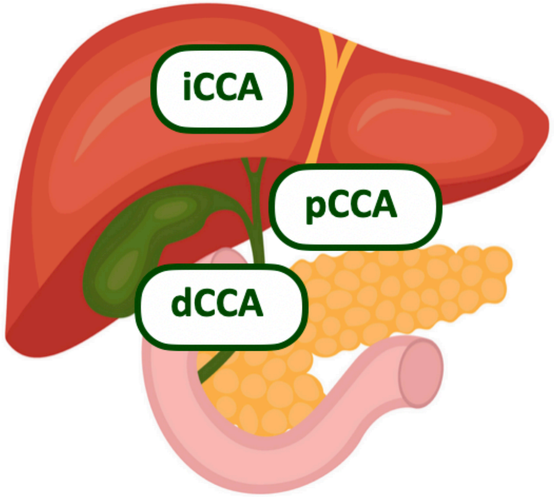

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Cholangiocarcinome et transplantation hépatique

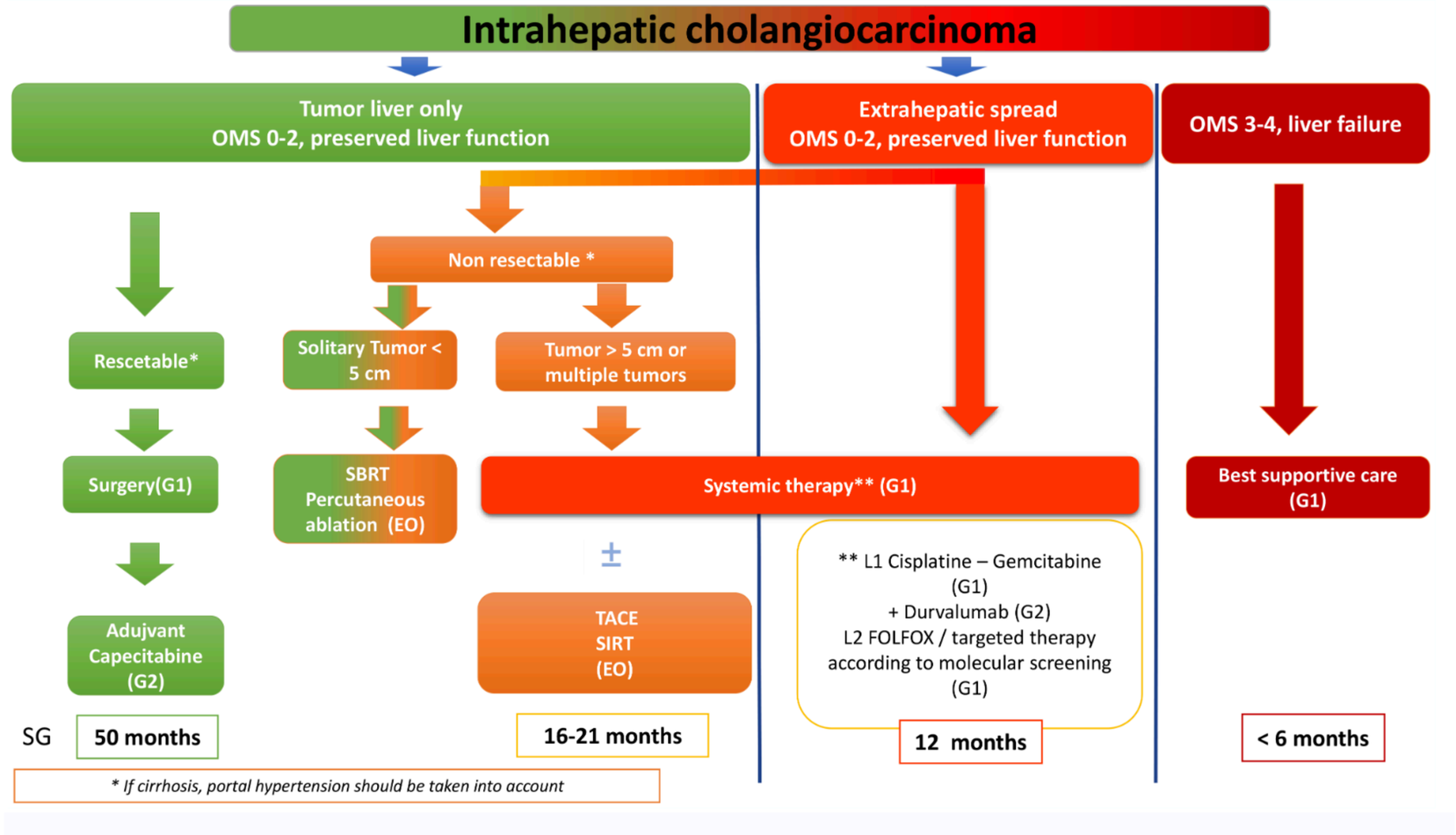
Table 2. Outcomes of liver transplantation for patients with intrahepatic cholangiocarcinoma: literature review.

Study	Year	Study design	n	Overall survival (%) 1-year	3-year	5-year	DFS (%) 5-year	Neoadjuvant treatment	Adjuvant treatment	Comments
Sotiropoulos *et al.*[95]	2008	Retrospective	10	70	50	33	–	none	none	–
Vallin *et al.*[96]	2013	Retrospective Multicentre	10	80	60	24	–	none	none	–
Sapisochin *et al.*[97]	2014	Retrospective Multicentre	27	78	66	51	36	none	none	–
Facciuto *et al.*[98]	2015	Retrospective	7 iCCA 9 iCCA+HCC 16 iCCA-HCC	71	–	57	44	none	none	–
Vilchez *et al.*[99]	2016	Retrospective Multicentre	440	79	58	47	–	none	none	–
Sapisochin *et al.*[100]	2016	Retrospective Multicentre	15 single ≤2 cm 33 multiple or >2 cm	93 79	84 50	65 45	82 39	none	none	–
O'Grady *et al.*[101]	1988	Retrospective	13 iCCA	38	10	10	no	none	none	–
Yokoyama *et al.*[102]	1990	Retrospective	2	50	0	–	–	none	none	–
Meyer *et al.*[103]	2000	Retrospective Multicentre	207	72	48	23	–	none	~10% of patients	84% DFS at 25 months.
Shimoda *et al.*[104]	2001	Retrospective	16	62	39	–	35	none	none	8 patients with iCCA-HCC.
Robles *et al.*[105]	2004	Retrospective Multicentre	23	77	65	42	–	none	none	2-year DFS 35%
Ghali *et al.*[106]	2005	Retrospective Multicentre	10	–	30	–	–	none	none	1 patient with iCCA-HCC
Hong *et al.*[107]	2011	Retrospective LR *vs.* LT	LT: 25 LR: 12	–	38	32	33	9 LT no LR	16 LT and 5 LR	–
Lunsford *et al.*[71]	2018	Prospective single-arm	12 enrolled 6 underwent LT	100	83.3	83.3	50	Chemotherapy + 6-month mandatory SD	none	–

DFS, disease-free survival; HCC, hepatocellular carcinoma; iCCA, intrahepatic cholangiocarcinoma; iCCA-HCC, mixed hepatocellular cholangiocarcinoma; LR, liver resection; LT, liver transplantation; SD, stable disease.

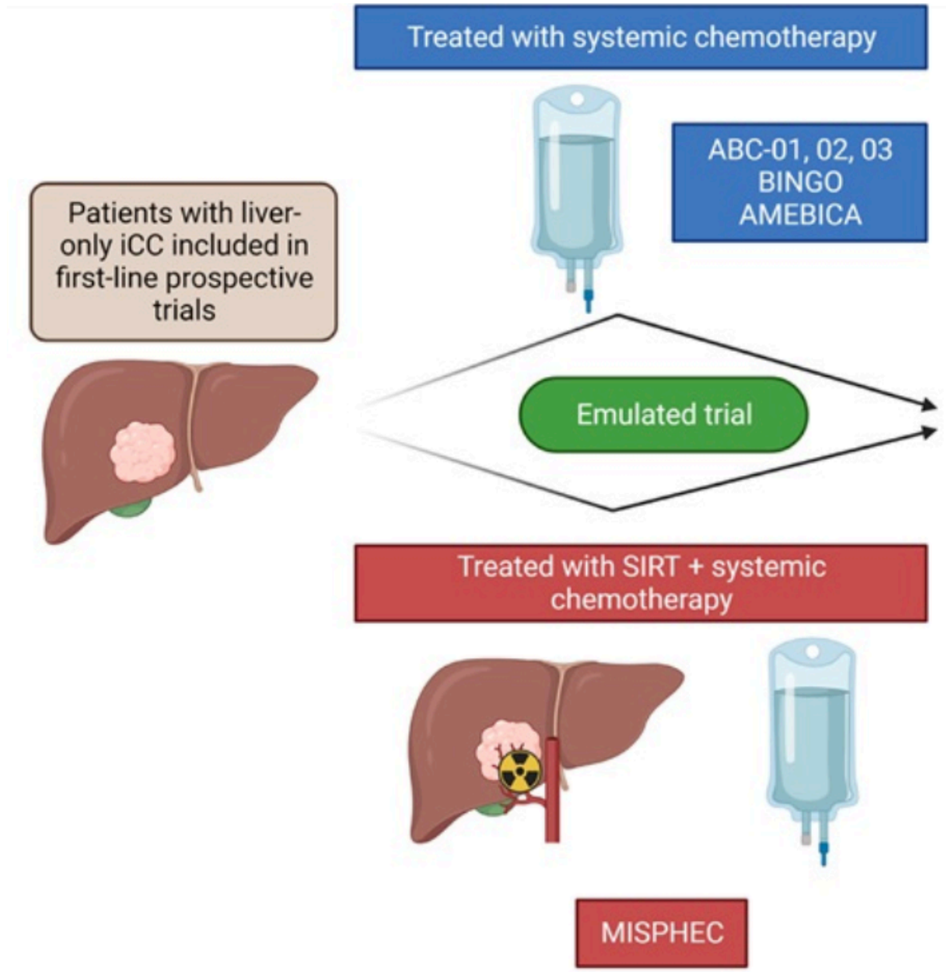
Mazzaferro et al. J Hepatol. 2020

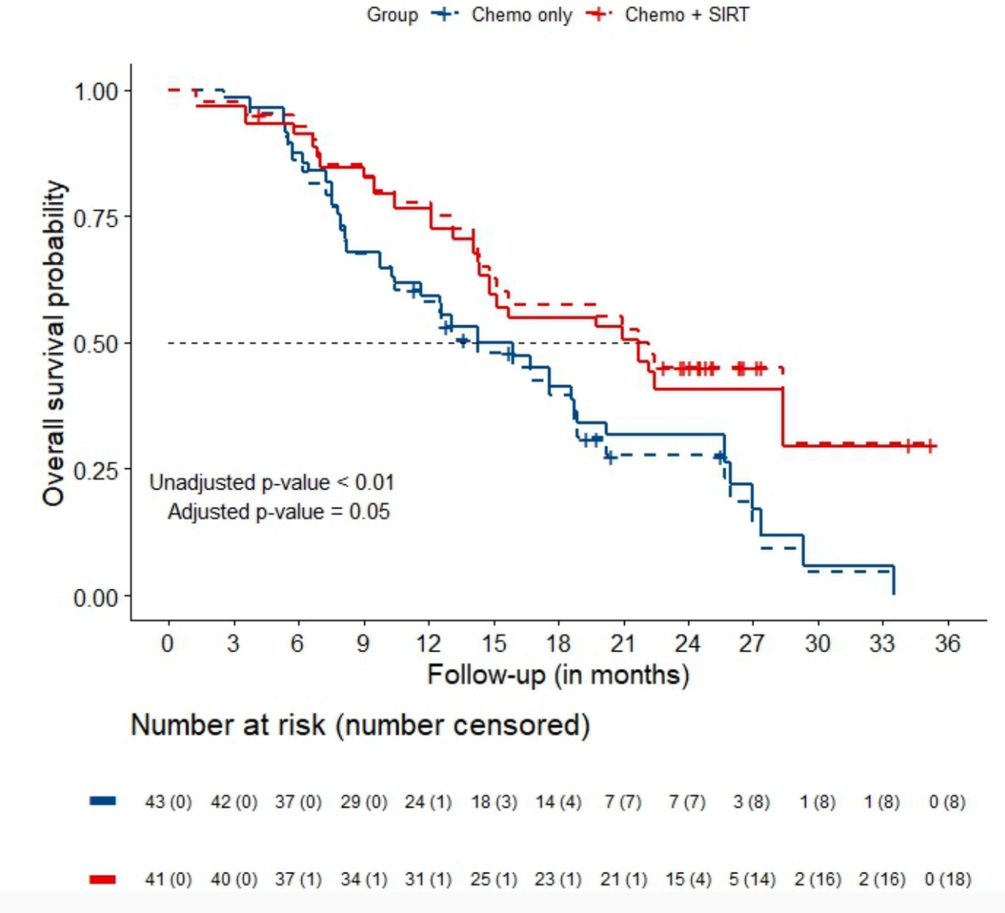
Stratégie thérapeutique



Neuzillet et al. Liver Int. 2024

Pourquoi la radioembolisation (SIRT) ? (1)

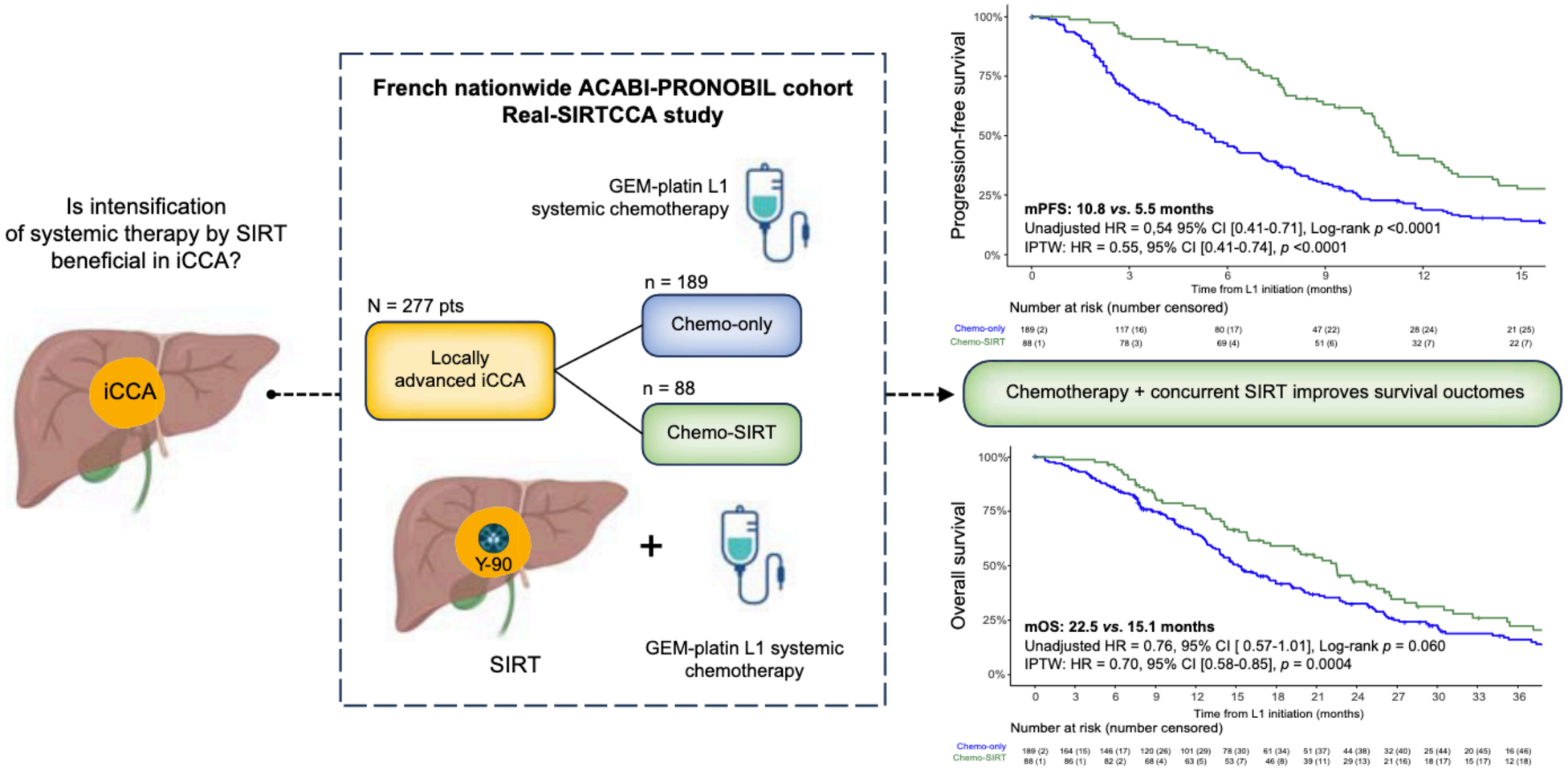




21.7 vs 15.9 mois
HR 0.59 [0.34-0.00]
p = 0.049

Edeline et al. Hepatology 2024

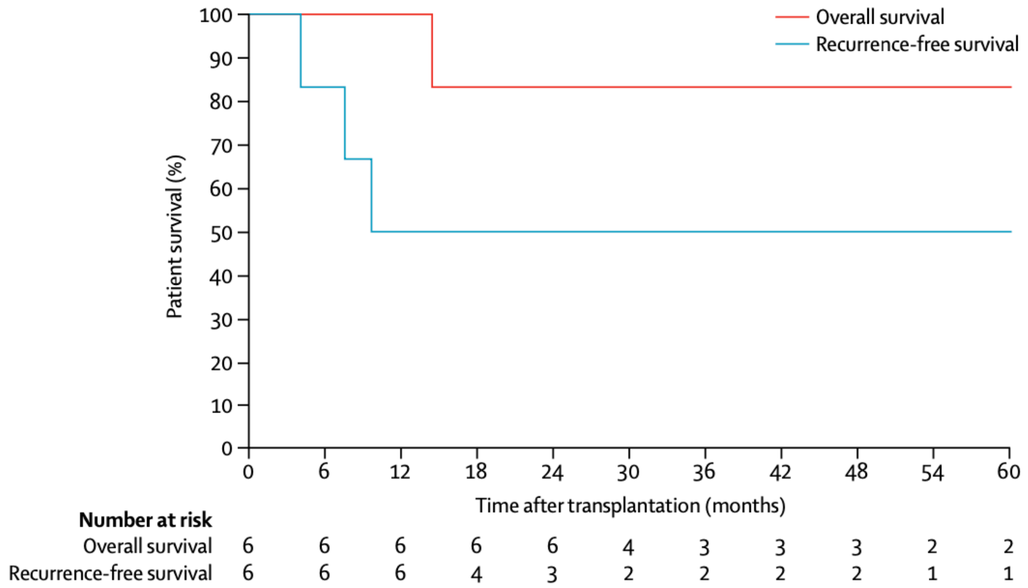
Pourquoi la radioembolisation (SIRT) ? (2)

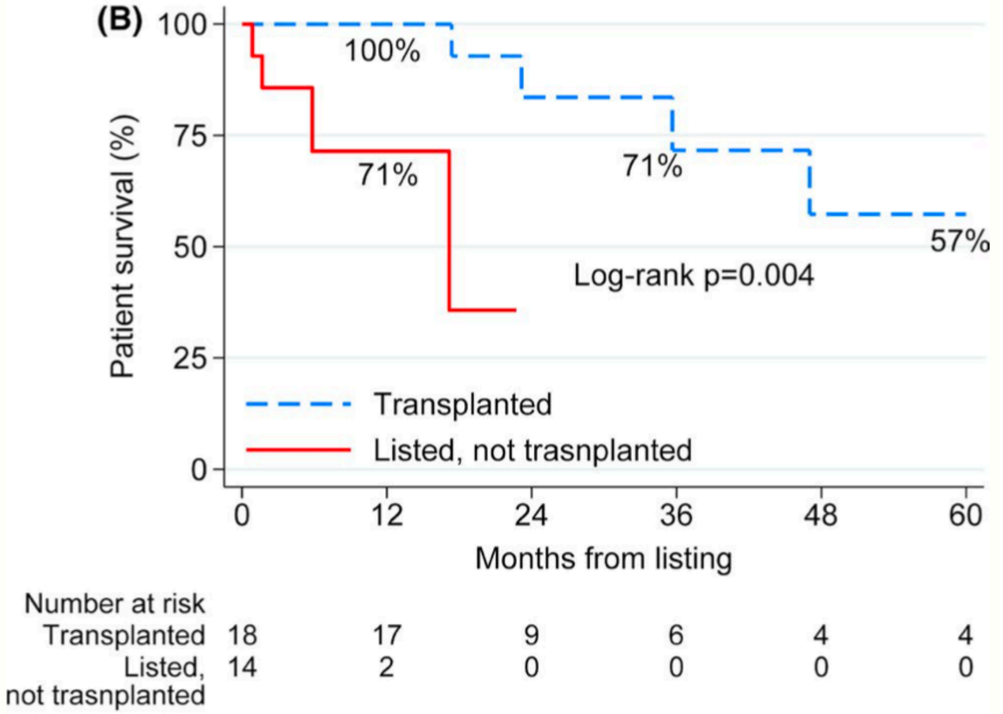


Adamus et al. JHEP reports 2025

Cholangiocarcinome et transplantation hépatique

- Intérêt du traitement néoadjuvant





Lunsford KE et al. Lancet Gastroenterol Hepatol 2018

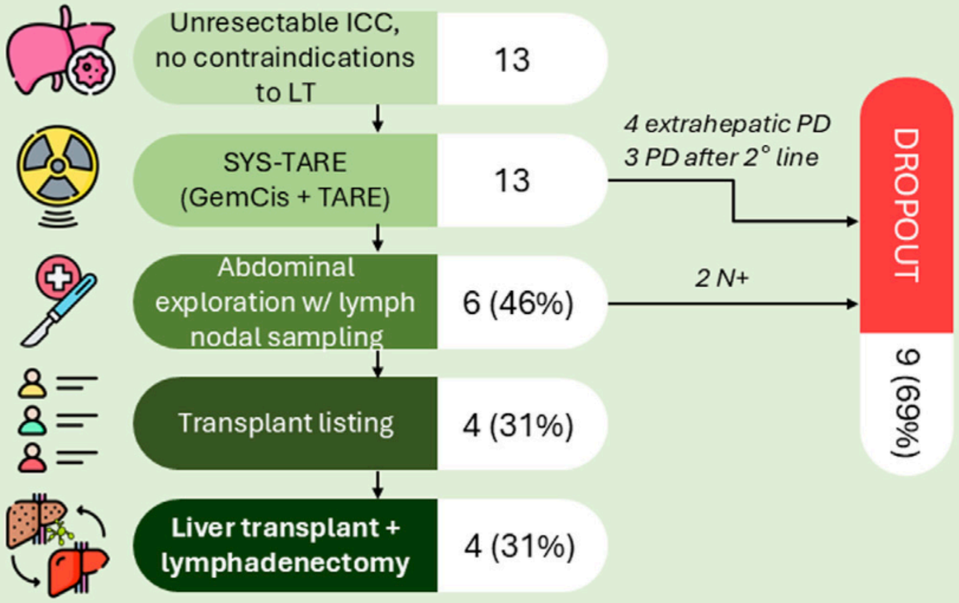
McMillan RR et al. Am J Transplant 2022

Cholangiocarcinome et transplantation hépatique

ReLleF

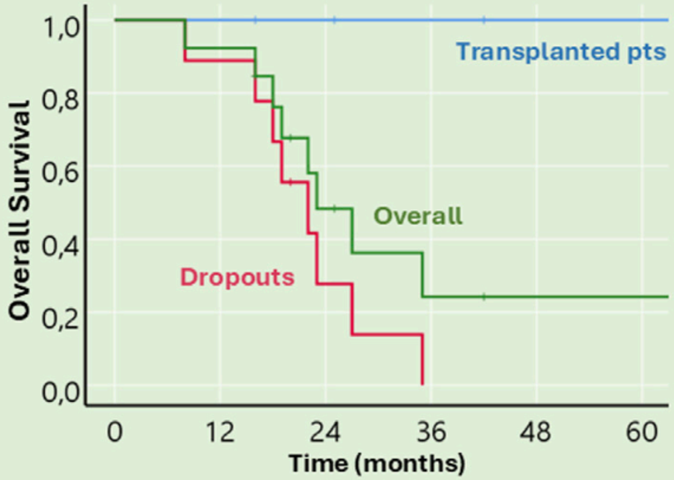
Liver Transplantation for Intrahepatic Cholangiocarcinoma after Chemotherapy and Radioembolization: an Intention-to-Treat Study

DOWNSTAGING PROTOCOL & INCLUDED PATIENTS



ONCOLOGICAL OUTCOMES

All transplanted patients are alive and disease-free at 73, 40, 12 and 8 months from transplant



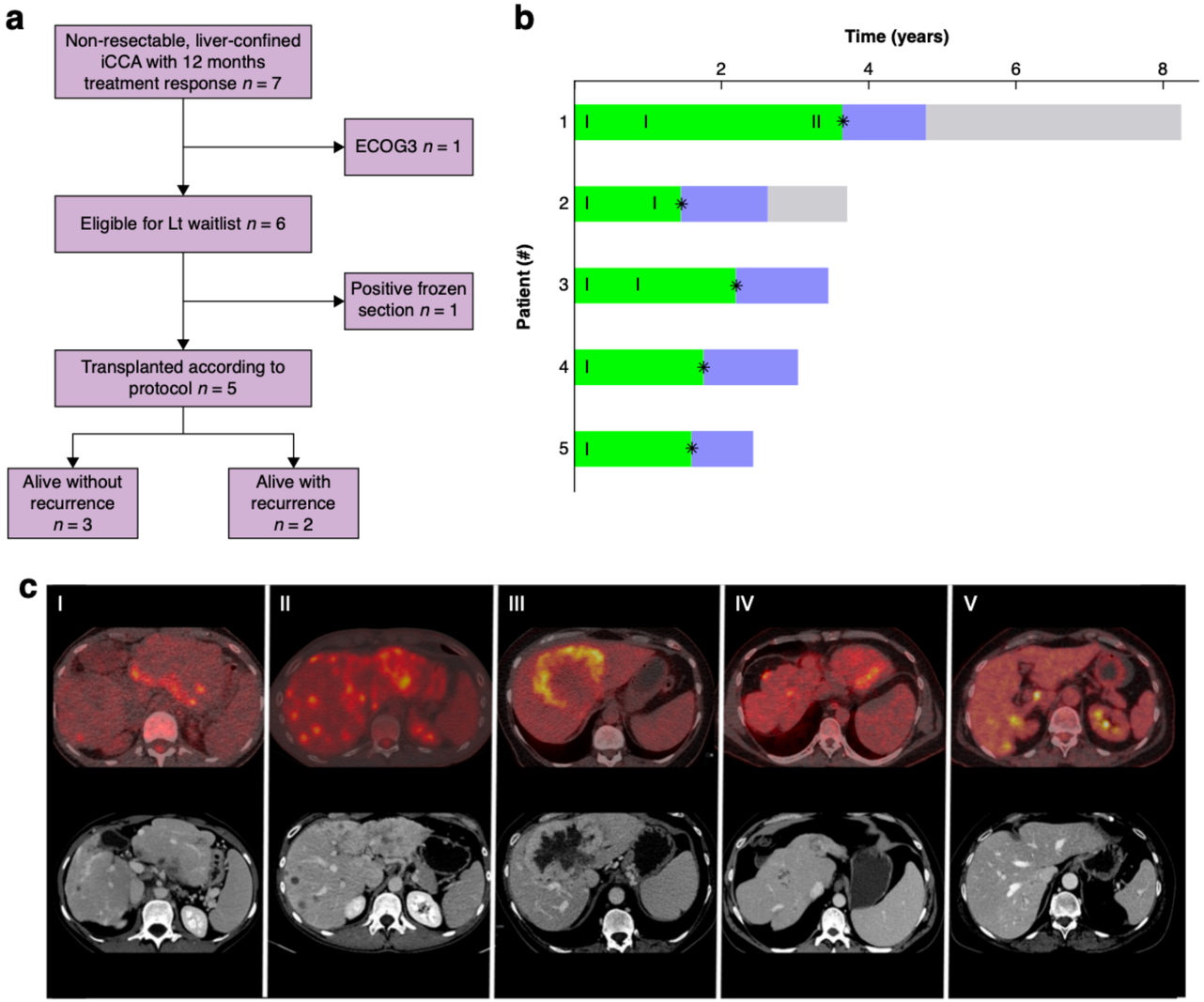
Transplant for iCC after downstaging with SYS-TARE is safe and feasible, with remarkable oncological outcomes

ESOT Leading the way in transplantation

Maspero, et al. *Transpl. Int.* 2024
doi: 10.3389/ti.2024. 13641

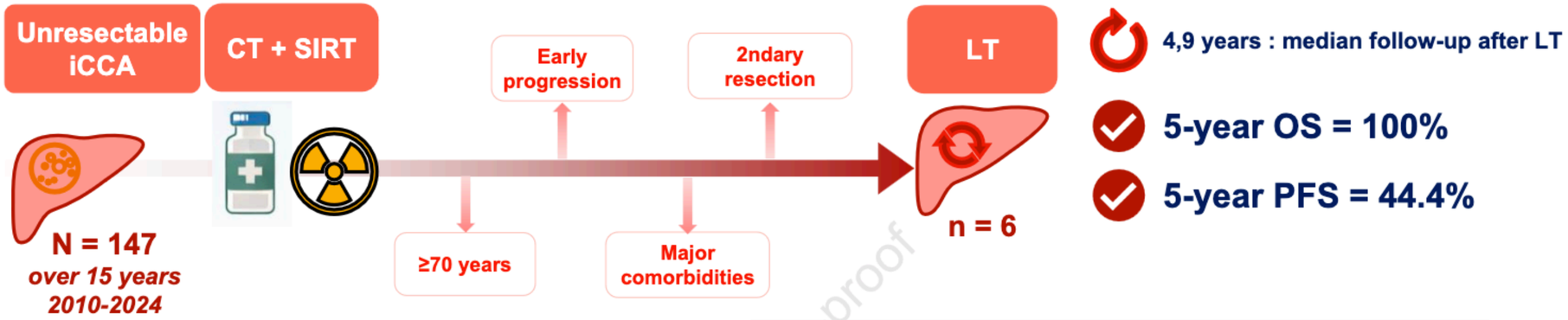
Transplant International

Cholangiocarcinome et transplantation hépatique



Yaqub S et al. BJS 2025

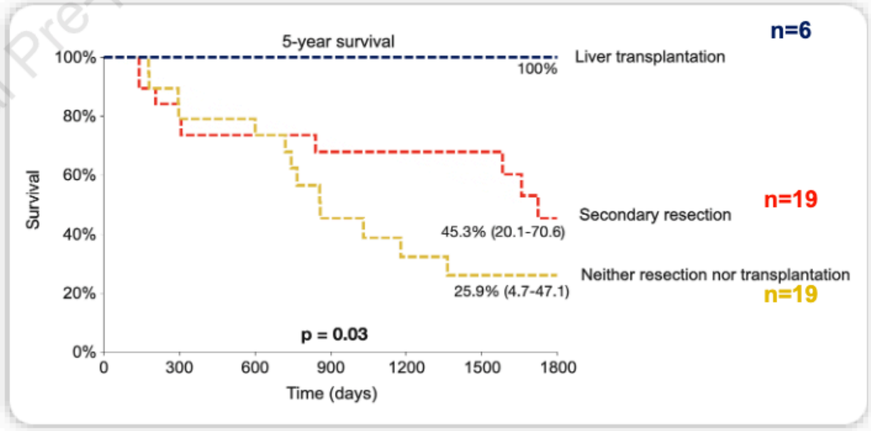
Cholangiocarcinome et transplantation hépatique



- 4,9 years : median follow-up after LT
- 5-year OS = 100%
- 5-year PFS = 44.4%

In liver transplantated patients

- 351 days : median timeframe from diagnosis to listing
- 114 days : median time from listing to LT



In a highly selected cohort of only six patients over 15 years, neoadjuvant SIRT combined with chemotherapy enabled favorable long-term outcomes after liver transplantation

CT, chemotherapy; **iCCA**, intrahepatic cholangiocarcinoma; **LT**, liver transplantation; **OS**, overall survival; **PFS**, progression-free survival; **SIRT**, selective internal radiation therapy.

Giguet B et al. JHEP reports 2026

OLT-iCCA : TH pour iCCA localement avancé, non résécable après traitement néoadjuvant par chimiothérapie et radioembolisation

ReLleF

- Etude **rétrospective** menée au CHU de Rennes + CEM.

- Incluant tous patients avec iCCA avancé, non résécable après traitement néoadjuvant comprenant obligatoirement l'association CT et SIRT.

- Période de recrutement : **2010 à 2024**

- Critère de jugement principal : **survie globale à 5 ans post TH**
- Critère de jugement secondaire : **survie sans récidive à 5 ans post TH**

OLT-iCCA : TH pour iCCA localement avancé, non résécable après traitement néoadjuvant par chimiothérapie et radioembolisation

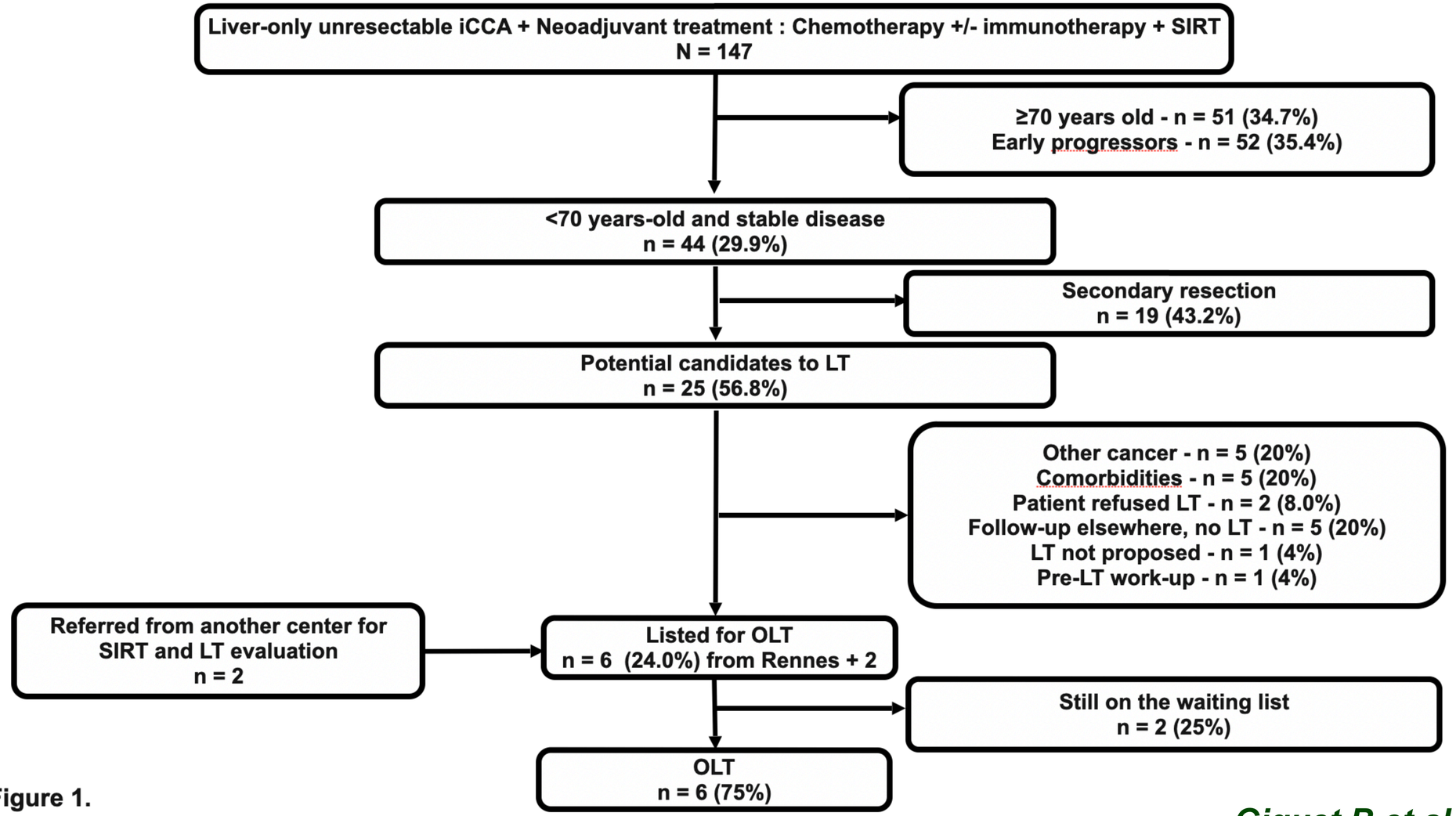


Figure 1.

Giguet B et al. JHEP reports 2026

Caractéristiques de la population (1)

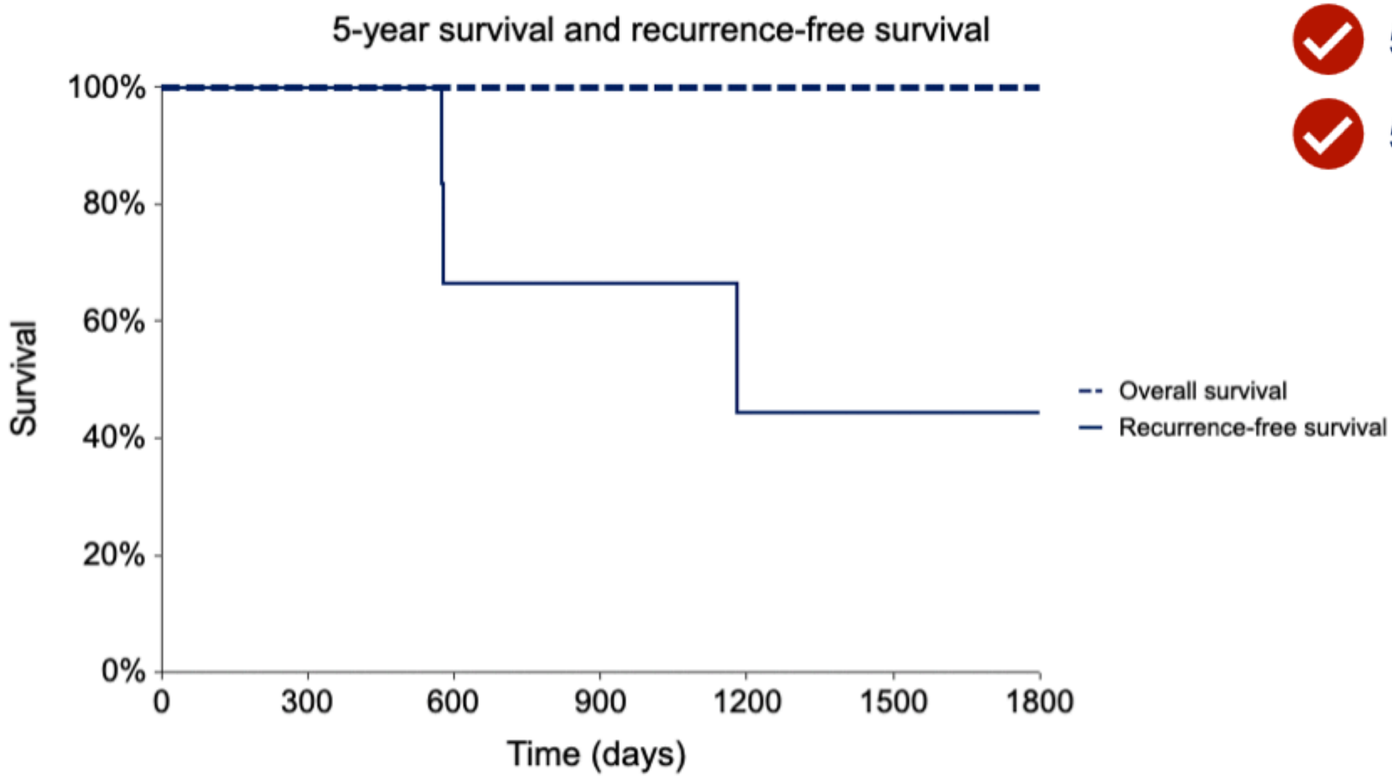
	Population N = 6
Patients' characteristics and liver transplantation variables	
Age, years	50.7 [39.9-59.3]
Sex, Female	3 (50.0%)
Body mass index, kg/m^2	23.2 [22.0-26.0]
Age adjusted Charlson comorbidity index	3 [3-4]
MELD at listing	7 [7-11]
Diabetes	0 (0%)
Hypertension	1 (16.7%)
Tobacco consumption	2 (33.3%)
Cirrhosis	2 (33.3%)
Delay between diagnosis and listing, days	351 [250-558]
Delay between listing and liver transplantation, days	114 [44-192]
Donor risk index	1.91 [1.5-2.1]
Age of the donor, years	65 [55-88]
Sex of the donor, Female	1 (16.7%)
Cold ischemia time, minutes	497 [403-512]

	Population N = 6
Tumors' treatments and characteristics	
Chemotherapy GEMCIS GEMCIS + DURVA LV5FU2 + CISPLATIN	 4 (66.6%) 1 (16.7%) 1 (16.7%)
Selective internal radiation therapy (SIRT)	6 (100%)
Lymph node sampling	5 (83.3%)
Total tumor size at baseline	100 [65-115]
Number of tumor nodules at baseline	1 [1-1]
Total tumor size at listing	80 [52-80]
Number of tumor nodules at listing	1 [1-1]
Total tumor size on explant	70 [52-90]
Number of tumor nodules on explant	1 [1-4]
Tumor differentiation on explant	1 [1-2]
Lymphatic invasion on explant	0 (0%)
Perinervous invasion on explant	1 (16.7%)
Vascular invasion on explant	2 (33.3%)

Table 3: Tumors' treatments and characteristics.

Giguet B et al. JHEP reports 2026

Données de survie (1)

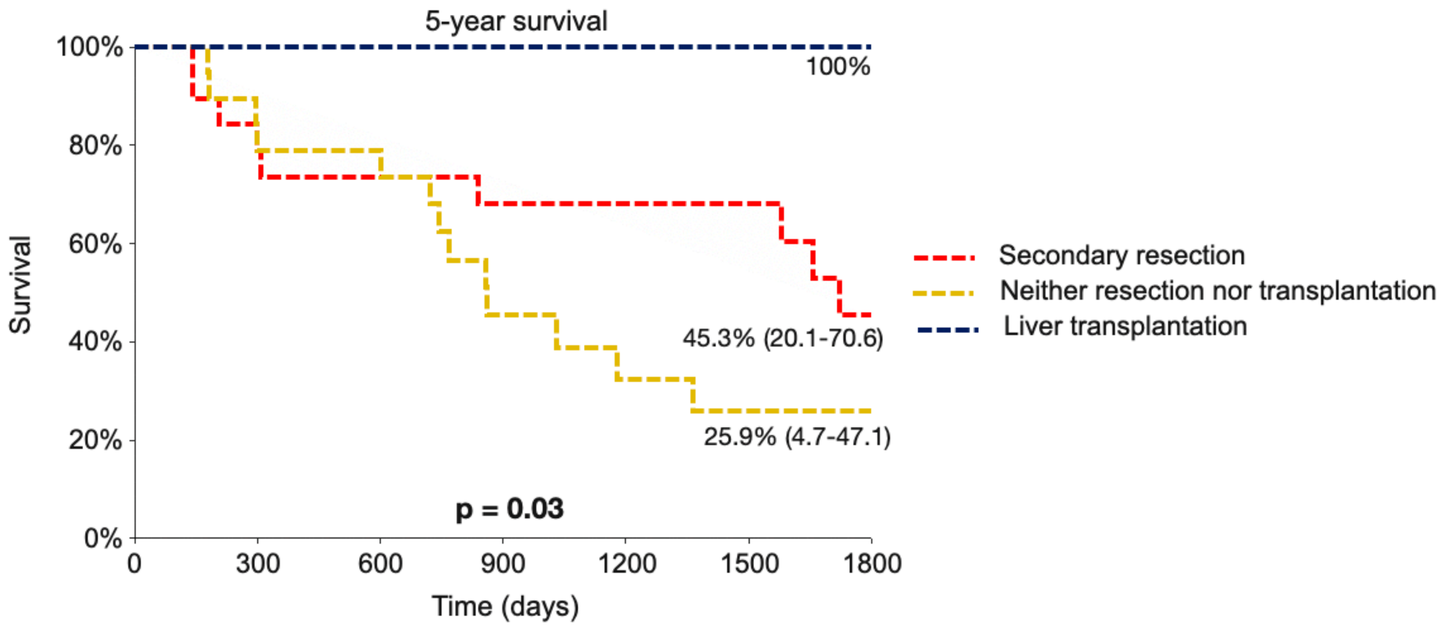


Number At Risk							
Overall survival	6	5	5	4	4	4	4
Recurrence-free survival	6	6	4	3	2	2	2

- **5-year OS = 100%**
- **5-year PFS = 44.4%**

Giguet B et al. JHEP reports 2026

Données de survie (2)



Number At Risk							
Secondary resection	19	15	14	12	11	9	6
Neither resection nor transplantation	19	15	15	8	5	4	4
Liver transplantation	6	5	5	4	4	4	4

Giguet B et al. JHEP reports 2026

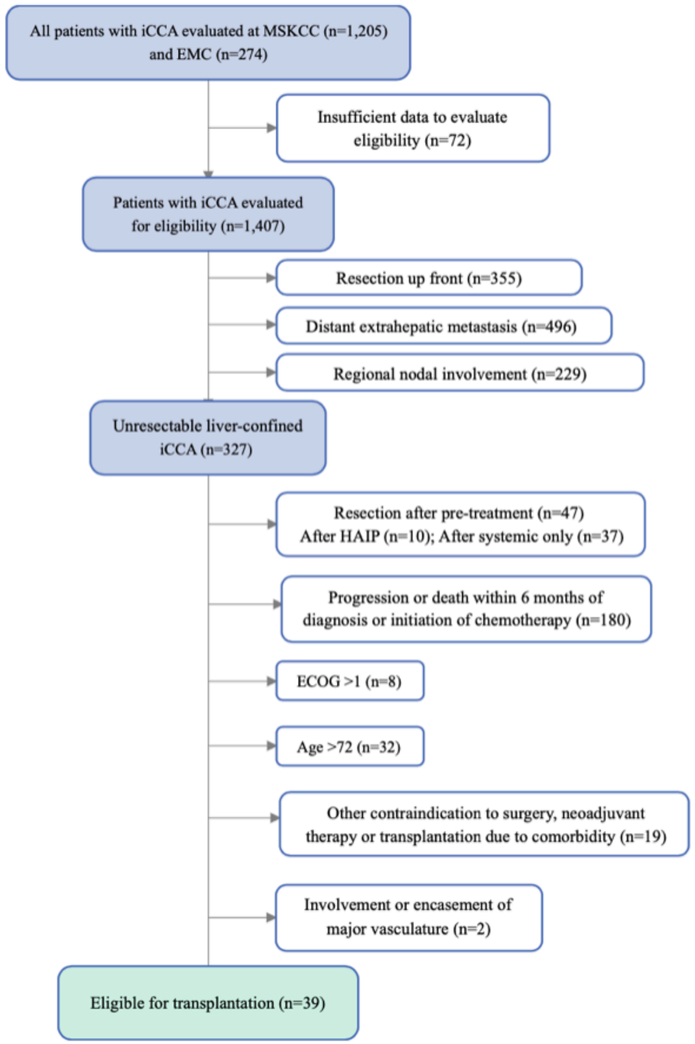
Evolution post TH

	Population N = 6
Outcomes	
Post-liver transplant hospitalization duration, days	12 [10-20]
Follow-up, years	4.9 [1.8–8.8]
Dindo-Clavien grade of complications 1 2 3b	 1 (16.7%) 4 (66.7%) 1 (16.7%)
Arterial complications	3 (50.0%)
Biliary complications	4 (66.7%)
Recurrence	3 (50%)
Time to reccurence, days	577 [573–33]
Sites of reccurence hepatic Extra hepatic	 0 3 (100%)

Table 4: Outcomes following liver transplantation.

Giguet B et al. JHEP reports 2026

Nombre de patients éligibles ?

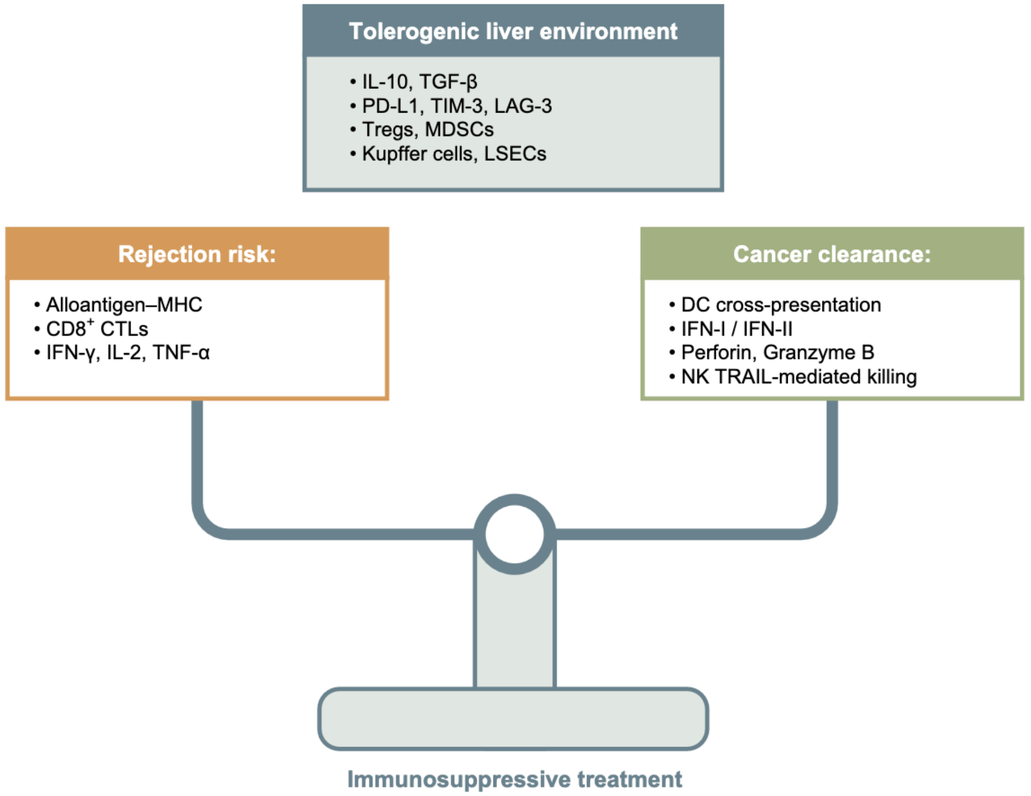


- 2 centres académiques (USA, NY)
- 2008 à 2018

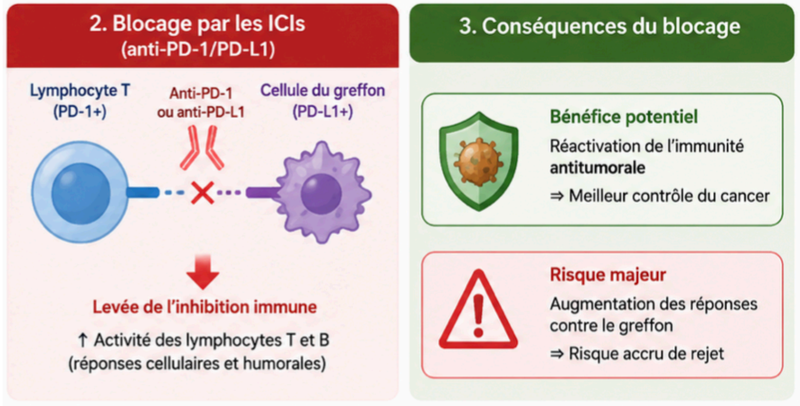
- 2.8% (39/1407) éligibles à la TH

Schleimer LE et al. Ann Surg Oncol. 2026

Particularités de l'onco - transplantation



- **Axe PD1 / PD-L1**
- Régulation activité immune (contrôle inhibiteur) :
  - Lymphocytes T : freinent la réponse immunitaire effectives
  - Lymphocytes B : inhibent la production de DSA



Wassmer CH et al. Hepatology. 2026

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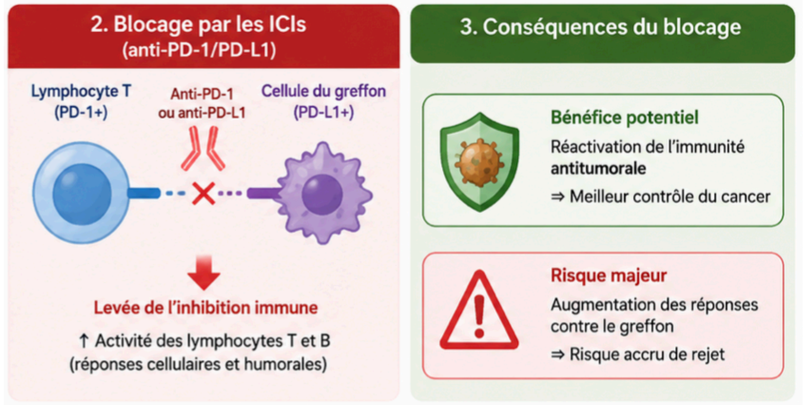


- **Période de WASH-OUT avant TH : 30 jours à 3 mois**

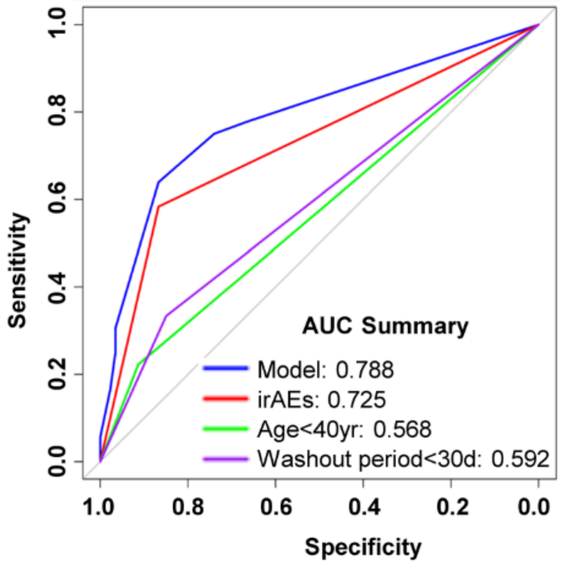
Wassmer CH et al. Hepatology. 2026
Rezaee-Zavareh MS et al. J Hepatol 2025
O’Kane G et al. AJT 2024

Particularités de l'onco - transplantation

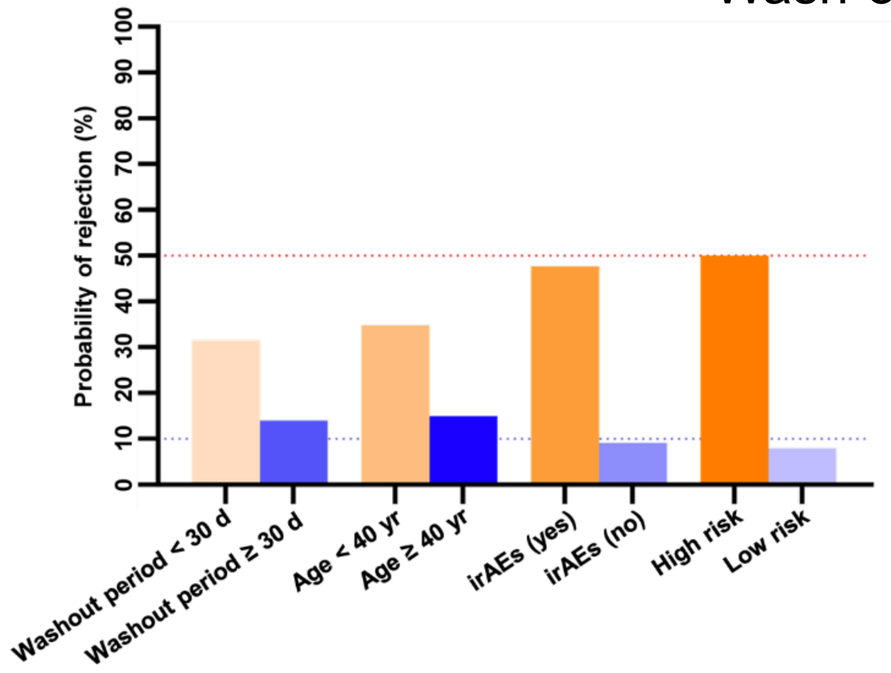
- **Population à risque de rejet**

- Age < 40 ans : OR 3.0 (1.0-9.1)
- **irAEs** (tout grade) : **OR 9.2** (4.0-21.0)
- Wash-out < 30 jours : OR 3.1 (1.2-7.8)

A



B

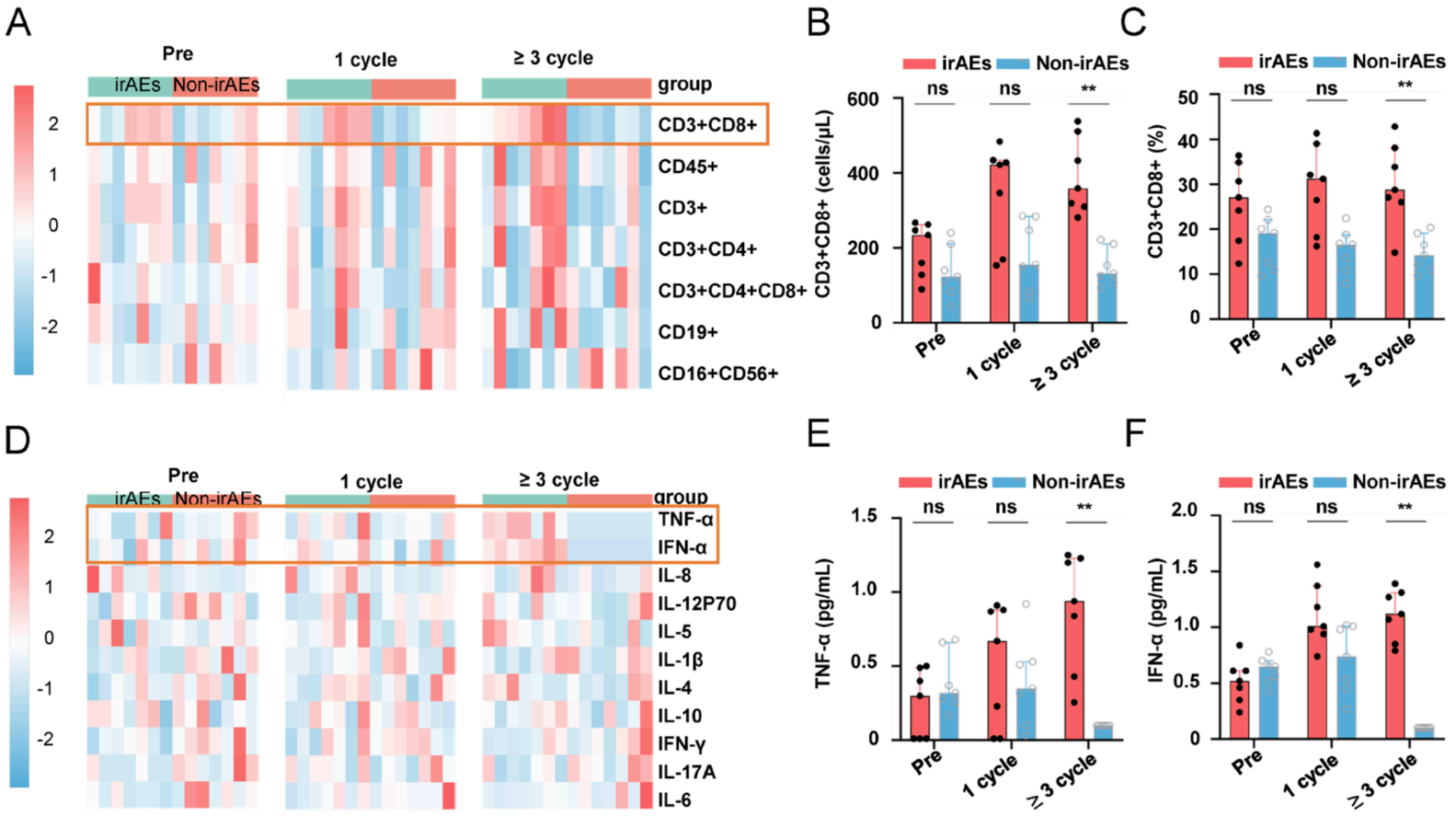


36/209 (17,2%) patients avec CHC traités par ICI ont présenté un rejet

Fang J et al. Gut 2025

Particularités de l’onco - transplantation

- **Population à risque de rejet**



Fang J et al. Gut 2025

Quelle IS après la greffe ?

Phase post-LT	General regimen (HCC, p/iCCA, CRLM, and NET)	Specific notes by tumor type
0–1 month	Tacrolimus 6–10 ng/mL ± MMF/steroids Basiliximab +MMF or AZA if renal risk Steroids taper by 1–3 months mTOR use limited (wound healing risk)	*HCC:* Minimize CNI in high recurrence or de novo cancer risk Consider mTOR for high risk (eg, MVI, poor differentiation) If recent ICI exposure: close surveillance, low threshold for biopsy, high dose corticosteroids if AR confirmed (add ATG if steroid-refractory) *pCCA-iCCA:* CNI minimization in high recurrence risk (mTOR use is rare/not first-line) *CRLM:* mTOR may start early if high risk (risk stratification: CEA, RAS/RAF, sidedness, volume, chemo response) *NET:* avoid mTOR in first month (if used, everolimus 3–8 ng/mL)
3–6 months	Tacrolimus 4–8 ng/mL (lower if combined) Steroids off mTOR or MMF if high recurrence risk	*HCC/pCCA-iCCA:* CNI regimen; consider mTOR only in select high-risk cases *CRLM:* consider mTOR monotherapy if stable *NET:* favor mTOR ± low-dose tacrolimus
> 1 year	Tacrolimus 3–5 ng/mL (minimized if combined) Consider CNI-free mTOR in high-risk tumors DSA monitoring and biopsy before CNI withdrawal	*HCC:* consider mTOR for MVI or poor differentiation *pCCA-iCCA:* standard CNI monotherapy; MMF or mTOR only in selected cases *CRLM*: mTOR target 5–8 ng/mL if combined or up to 10–12 ng/mL if monotherapy *NET:* aggressive CNI minimization, mTOR monotherapy if high-risk

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Conclusion

- La survie globale à 5 ans des patients transplantés hépatiques pour iCCA localement avancé, non résécable après traitement par SIRT plus chimiothérapie, suggère un réel bénéfice thérapeutique individuel, tout en conservant une utilité sur le plan collectif.

- La stratégie néoadjuvante incluant la SIRT pourrait participer à ces bons résultats et mérite d'être investiguée dans une cohorte de plus large effectif.

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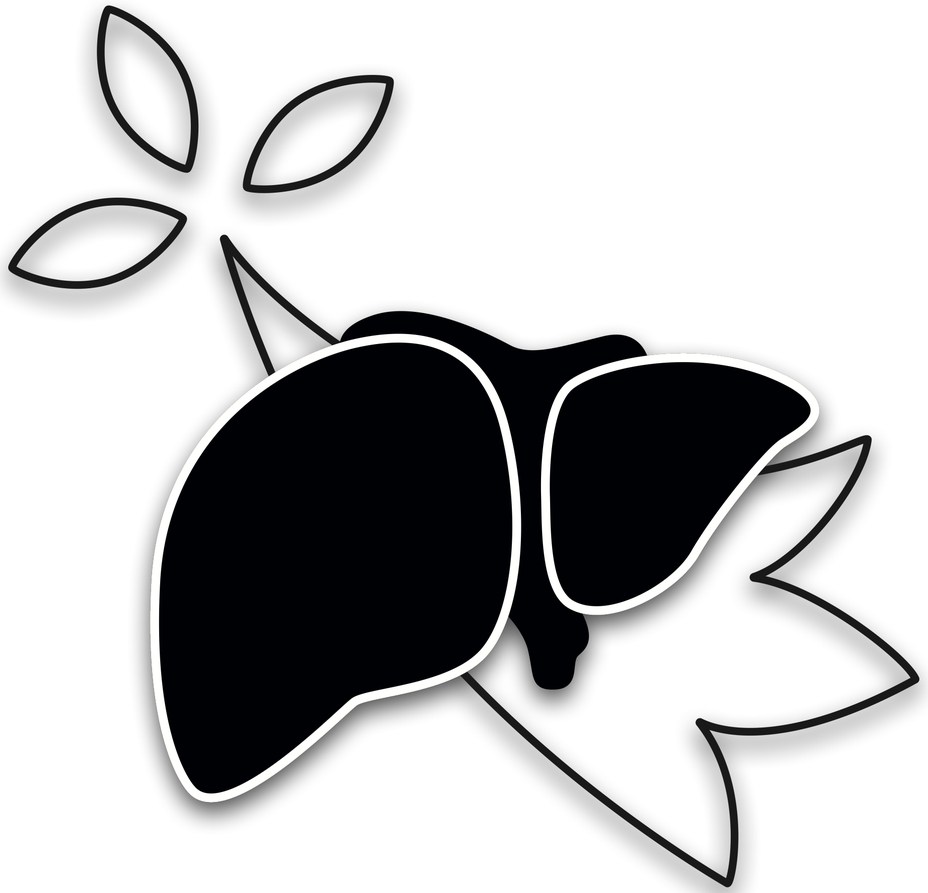

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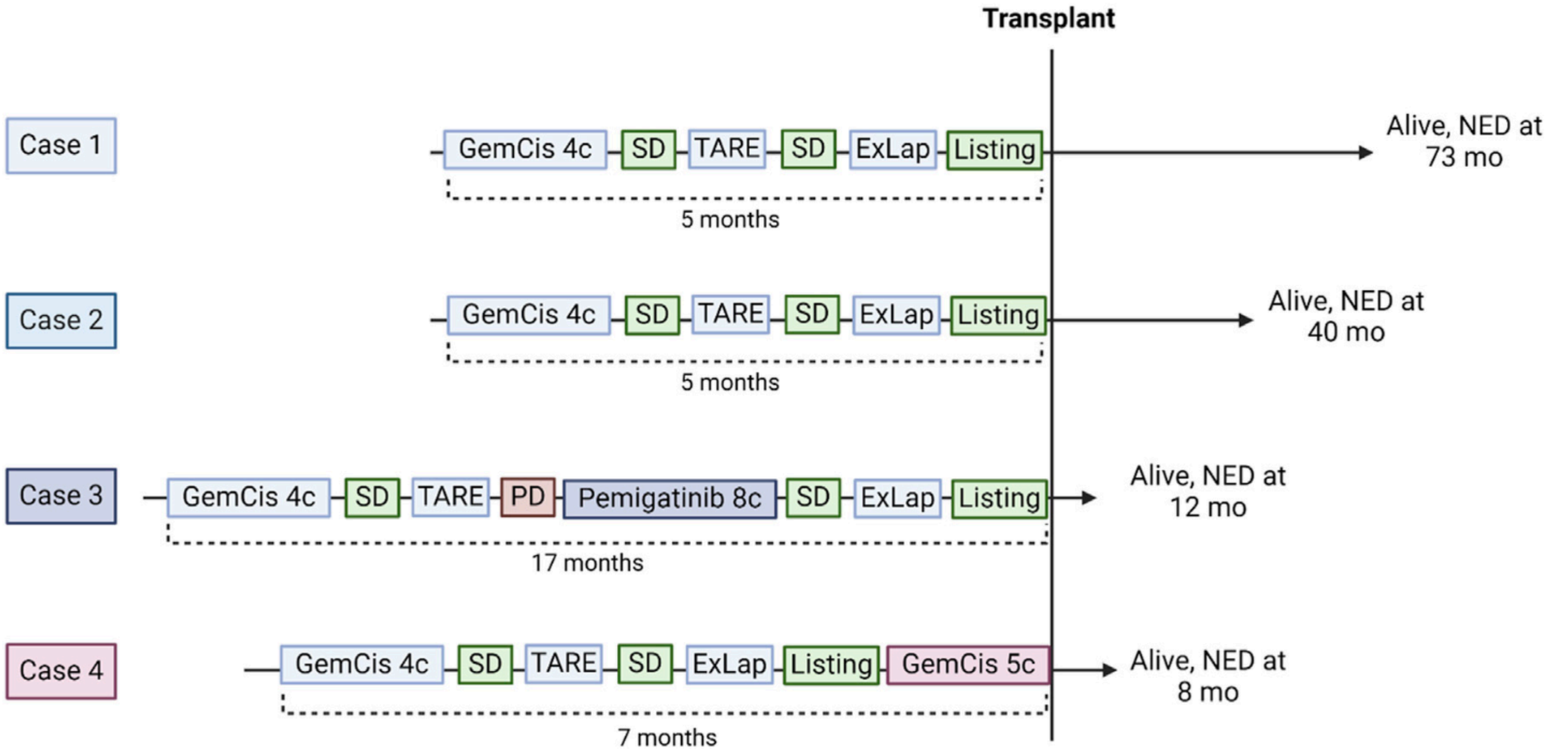

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Nombre de patients éligibles ?

Table 1 (continued)

Characteristic	Overall, N = 327[a]	Resected after neoadjuvant treatment, N = 47[a]	Unresectable, eligible for liver transplant, N = 39[a]	Unresectable, not eligible for liver transplant, N = 241[a]	P^{b}
BAP1	18/105 (17%)	4/33 (12%)	6/20 (30%)	8/52 (15%)	0.2
BRAF	7/108 (6.5%)	2/33 (6.1%)	1/22 (4.5%)	4/53 (7.5%)	>0.9
CDKN2A	2/105 (1.9%)	0/33 (0%)	1/20 (5%)	1/52 (1.9%)	
FGFR2	4/105 (3.8%)	0/33 (0%)	1/20 (5%)	3/52 (5.8%)	
FGFR3	0/1 (0%)	0/0 (NA%)	0/1 (0%)	0/0 (NA%)	
IDH1	19/107 (18%)	8/33 (24%)	1/21 (4.8%)	10/53 (19%)	0.2
IDH2	6/107 (5.6%)	1/33 (3.0%)	1/21 (4.8%)	4/53 (7.5%)	
KRAS	10/109 (9.2%)	2/33 (6.1%)	1/22 (4.5%)	7/54 (13%)	0.5
PBRM1	10/105 (9.5%)	5/33 (15%)	0/20 (0%)	5/52 (9.6%)	0.2
TP53	18/106 (17%)	5/33 (15%)	4/21 (19%)	9/52 (17%)	>0.9
NRAS	4/108 (3.7%)	1/33 (3%)	1/22 (4.5%)	2/53 (3.8%)	
ERBB2	1/108 (0.9%)	1/33 (3%)	0/22 (0%)	0/53 (0%)	
FGFR2.fus	16/105 (15%)	8/33 (24%)	4/20 (20%)	4/52 (7.7%)	0.09

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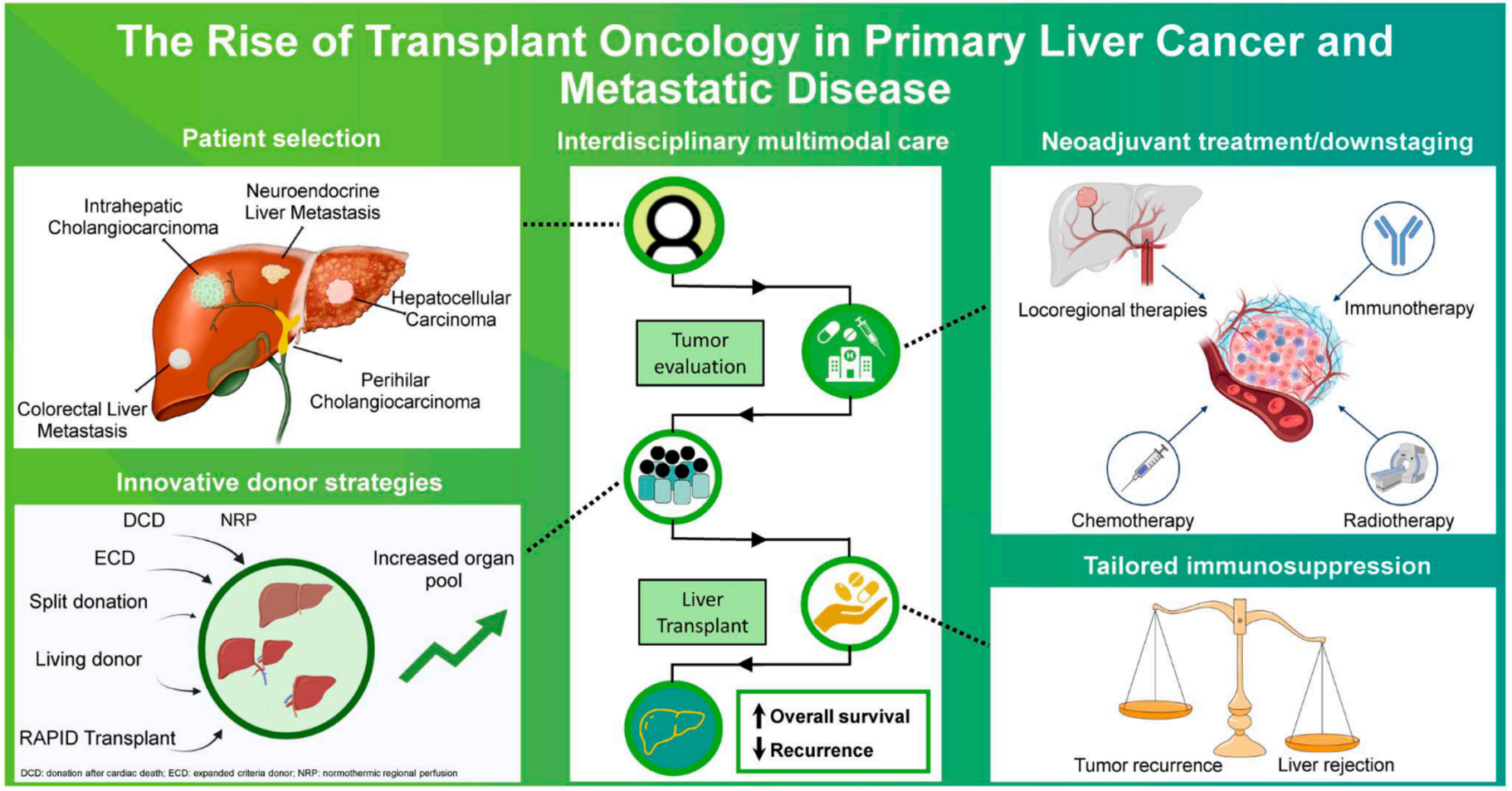
Particularités de l’onco - transplantation



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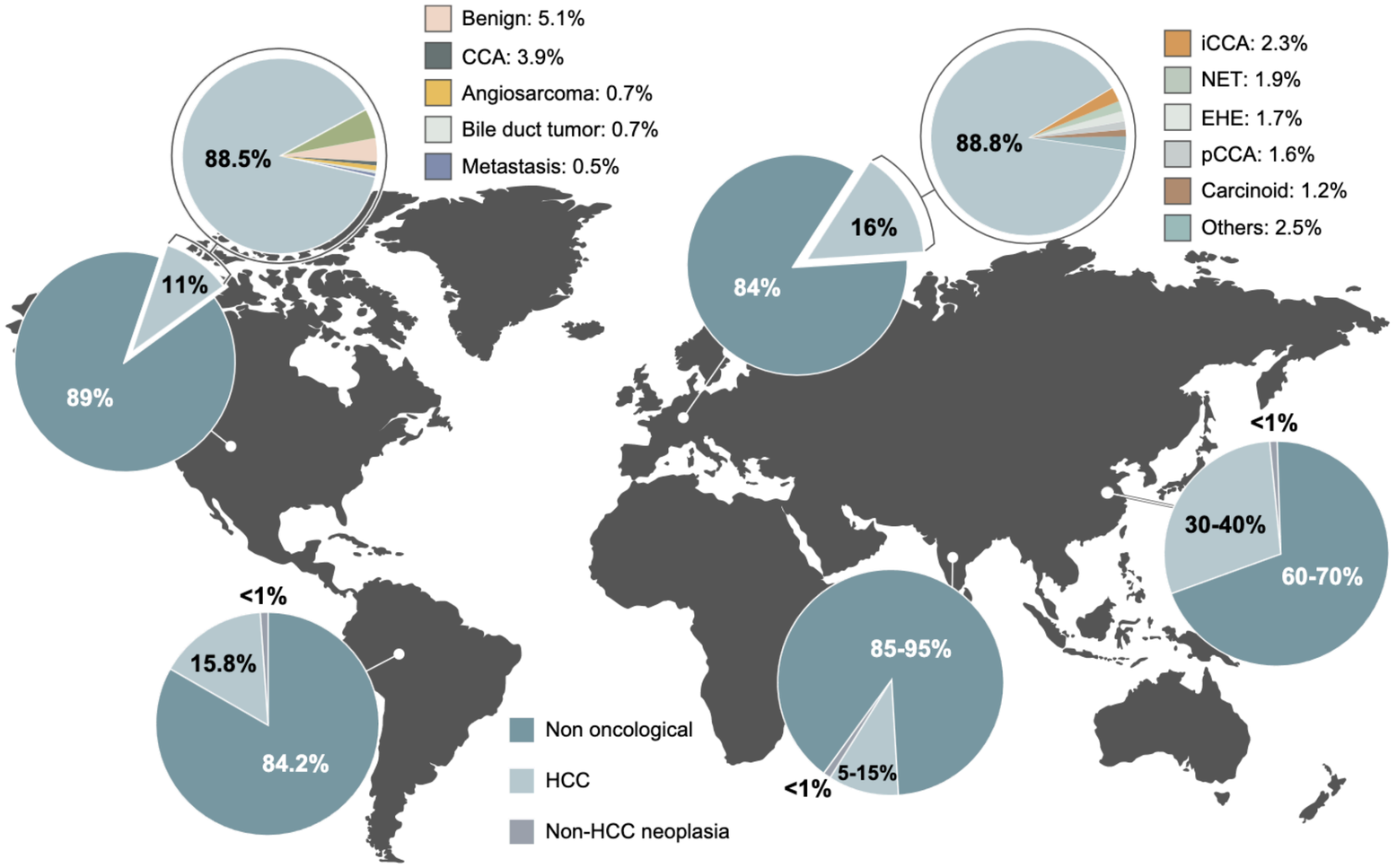

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Particularités de l'onco - transplantation

TABLE 2 iCCA indications and contraindications for liver transplantation

Category	Criteria	
	Indications	**Contraindications**
Very early iCCA	Single lesion ≤2–3 cm in diameter Underlying cirrhosis Not amenable to resection due to portal hypertension or liver dysfunction	–*Extrahepatic metastasis:* Lymph node Peritoneal Distant organ involvement – *Vascular invasion:* Macrovascular or major vessel invasion (eg, portal vein, hepatic veins) – *Tumor progression:* Radiological or biochemical progression during neoadjuvant therapy –*High tumor burden:* Multifocal disease not amenable to downstaging Misclassified perihilar cholangiocarcinoma – *Poor performance status:* ECOG ≥2 or significant comorbidities limiting transplant candidacy – *Prior treatment failure:* Rapid progression or recurrence after previous surgical or oncologic therapy Other established contraindications to liver transplantation
Locally advanced iCCA	Unresectable due to tumor location or multifocality No extrahepatic spread No macrovascular invasion Sustained radiologic stability or partial response to neoadjuvant therapy for ≥6 months	
Favorable biology	Low-grade histology Absence of aggressive molecular markers (under investigation) Stable tumor markers (eg, CA 19-9)	
Controlled protocol	Managed within a prospective trial or institutional transplant protocol	

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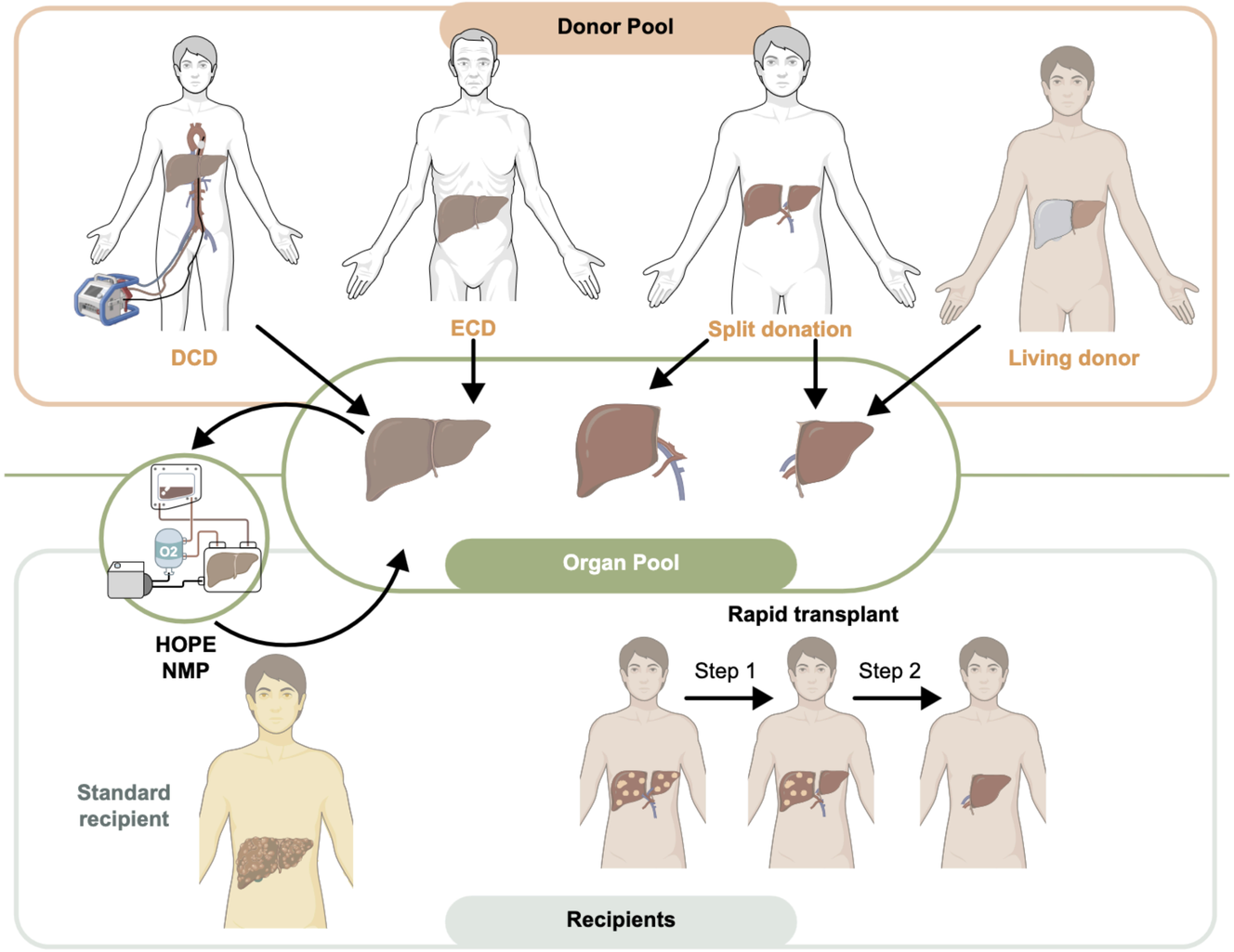
Particularités de l’onco - transplantation



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